REMARKS/ARGUMENT

The Examiner is thanked for many explanatory comments in the Office Action which have greatly helped to define the remaining objections. The Examiner is also thanked for pointing out the allowability of claim 96, subject to adding language showing synergy between the precursor and the selective estrogen receptor modulator. That language has now been added to independent claim 2 from which claim 96 depends. Therefore, claim 96, through its dependency, now incorporates the synergy language that the Examiner has requested.

The other amendments are for simplifying the language and are not believed to change the scope of the claims.

Disclosure Objection

Applicant inadvertently mailed four additional Figures (10-13) which were not intended to be a part of this patent application and were not part of the parent application of which the present application is a continuation. Figures 10-13 are therefore being canceled. The brief description of Figs. 1-9 now corresponds to the actual Figures in the application.

Art Rejection

The references cited by the Examiner for the proposition that SERMs are known to have an anti-cholesterol effect are instead references which suggest the use of antiestrogens (also known as estrogen-receptor antagonists) against diseases that are exacerbated by estrogen-receptor activation. In other words, if a disease is known to respond unfavorably to estrogen-receptor activation, then compounds known to block the estrogen receptor so that it may not be activated by estrogen are taught to be useful for that purpose. By contrast, sex steroid precursors are known to be converted to the sex steroids -- both androgens and estrogens, depending on the enzymes available in the particular tissue in question. One of skill in the art would not have been motivated to combine the references related to sex steroid precursors (which can produce estrogen *in vivo*) with references relating to antiestrogens. One of skill in the art would not have

been led by the references to combine a compound capable of causing estrogen-receptor activation (sex steroid precursors) with other compounds designed to prevent estrogen receptor activation (estrogen antagonists, also known as antiestrogens). The skilled artisan would have expected the two components to work against each other rather than synergistically.

Labrie '201 discusses antiestrogens -- not selective estrogen receptor modulators. The art would not have been motivated by Labrie '201 to use its compounds other than to suppress estrogen receptor activation. It wasn't until later that the compounds of Labrie '201 were found to be selective estrogen receptor modulators. Even then, the effect of selective estrogen receptor modulators on cholesterol, when used in combination with sex steroid precursors as claimed herein, was not predictable. Selective estrogen receptor modulators, by definition, are compounds which work analogously to estrogens in some tissues while working analogously to anti-estrogens (or estrogen-receptor antagonists) in other tissues. It was not predictable, from the cited prior art, whether selective estrogen receptor modulators would work synergistically with sex steroid precursors, or whether they would be counterproductive. Until applicant actually tried the combination and tested the result on cholesterol, the beneficial results shown by applicant's data could not have been predicted. For this reason, it is urged that the references cited by the Examiner, neither alone, nor in combination, set forth a *prima facie* case of obviousness.

Even if a *prima facie* case was made, the Examiner is thanked for acknowledging that applicant's previously-submitted data establishes an unexpected synergy, except for the Examiner's concern that the scope of the claims exceeded the showing of the data by not requiring synergy in the claim language. In response to the Examiner's concerns, all claims (either directly or though their dependencies) have now been amended to provide the further claim language requested by the Examiner.

Accordingly, for all of the foregoing reasons, it is urged that the Examiner's rejection at 35 U.S.C., § 103 should be withdrawn.

It is believed that the application is now in condition for allowance. Issuance of a Notice of Allowance is solicited.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Mail Stop Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on May 5, 2003:

William O. Gray, III
Name of applicant, assignee or Registered Representative

Signature

May 5, 2003
Date of Signature

WOG:db

Respectfully submitted,

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APPENDIX A

"CLEAN" VERSION OF EACH PARAGRAPH/SECTION/CLAIM
37 C.F.R. § 1.121(b)(ii) AND (c)(i)

SPECIFICATION:

In the Drawings

Delete Figures 10-13.

CLAIMS (with indication of amended or new):

(AMENDED) 2. A method of treating or reducing the risk of acquiring hypercholesterolemia comprising administering to a patient in need of such treatment or reduction a therapeutically effective amount of a sex steroid precursor selected from the group consisting of dehydroepiandrosterone, dehydroepiandrosterone-sulfate, androst-5-ene-3β,17β-diol and a compound converted in vivo to one of the foregoing, and further comprising administering to said patient a therapeutically effective amount of a selective estrogen receptor modulator as part of a combination therapy; wherein a beneficial effect of said combination exceeds, by a statistically significant margin, a beneficial effect from either said precursor or said selective estrogen receptor modulator alone.

APPENDIX B

VERSION WITH MARKINGS TO SHOW CHANGES MADE
37 C.F.R. § 1.121(b)(iii) AND (c)(ii)

SPECIFICATION:

In the Drawings:

Delete Figures 10-13.

CLAIMS:

Claim 2: A method of treating or reducing the risk of acquiring hypercholesterolemia comprising [increasing levels] administering to a patient in need of such treatment or reduction a therapeutically effective amount of a sex steroid precursor selected from the group consisting of dehydroepiandrosterone, dehydroepiandrosterone-sulfate, androst-5-ene-3β,17β-diol and a compound converted in vivo to [thereof, in a patient in need of said treatment or said reduction by administering said steroid precursor to said patient] one of the foregoing, and further comprising administering to said patient a therapeutically effective amount of a selective estrogen receptor modulator as part of a combination therapy; wherein a beneficial effect of said combination exceeds, by a statistically significant margin, a beneficial effect from either said precursor or said selective estrogen receptor modulator alone.